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REMARKS

Claims 84 -98 and 100-110 are pending in this application. Claims 1-83 and 99 have been canceled without prejudice or disclaimer. Claim 110 has been newly added.

Claims 84-98, 101-102, and 105-108, have been amended to place them in better U.S. format. No new matter has been added.

Claims 101 and 102 have been amended to replace "medical disorders" with "physiological disorders" so as to provide further antecedent basis to the claims. No new matter has been added.

Applicants thank the Examiner for indicating claims 85-95, 98 and 104-107 allowable if rewritten in independent form to include all of the limitations of the base claim and any intervening claims.

Applicants thank the Examiner for pointing out the amendments to be made to claims 84-95, 98, 99, 105 and 107. Applicants have amended claims 84-95, 98, 99, 105 and 107 accordingly. No new matter has been added.

In view of the following, further and favorable consideration is respectfully requested.

- I. ***At page 2 of the Official Action, claims 100-103 and 109 have been rejected under 35 USC §112, first paragraph as failing to comply with the enablement requirement.***

The Examiner asserts that the instant invention is directed to treatment or detection of physiological disorders, such as tumors/cancers. The Examiner states that due to the vast range of cellular mechanisms characterizing types of cancer it is impossible to assume the method of the invention is capable of treating or detecting

all various types of cancers without performing undo experimentation. Furthermore the Examiner asserts that it is unclear which physiological disorders are intended.

In view of the following, this rejection is respectfully traversed.

Applicants respectfully agree with the assertion that characterization of cancer and other diseases is diverse. Applicants respectfully point out that the present subject matter is directed to **detection** and **not** to treatment of a specific, well defined, phenomenon manifested in a defined group of physiological disorders. This phenomenon is the perturbation of the normal organization of the cell plasma membrane (PNOM) which has been established in the art as an intrinsic cellular mechanism manifested in a plurality of physiological disorders (Martin S., et al., J. Exp. Med., 182:1545-1556, 1995; Bratton, D. L., et al., J. Biol. Chem., 272:26159-26165, 1997 cited in the specification). The described subject matter is directed to a method for detecting this phenomenon by contacting perturbed membrane cells employing the compounds disclosed in the application.

PM cells and physiological disorders characterized by the presence of these cells, are described in detail in the specification at, for example, pages 13-14 and 16-17, as well as in the claims as originally filed.

Claim 100 recites a method for detecting physiological disorders intrinsically characterized by perturbed membrane cells as recited: "*A method for the detection of physiological disorders characterized by the presence of cells having perturbed membranes (PM cells)*". According to claim 100 the physiological disorder is detected by administering a diagnostic agent operative to selectively bind to PM cells. Applicants do **not** recite a method for treating cancers or physiological disorders, rather the present subject matter describes a method for detecting the intrinsic cellular mechanism manifested in physiological disordered characterized by

the occurrence of PM cells. Thus claims 100-103 and 109 are well defined and a person skilled in the art can readily perform the method recited in the claims 100-103 and 109 without undue experimentation.

In view of the foregoing, it is submitted that claims 100-103 and 109 are fully enabled within the meaning of 35 USC § 112, first paragraph. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

II. *At page 6 of the Official Action, claims 84, 96, 97, 99, 100, 108, and 109, have been rejected under 35 USC §112, second paragraph as being indefinite.*

The Examiner asserts that claim 84 is indefinite because "R" is not defined; because it contains improper Markush terminology; and because it is unclear what labels are claimed to be compatible with the instant invention. With regard to claim 96, the Examiner asserts that this claim is ambiguous because of the phrase "said metal being comprised within the Q moiety of the compound of claim 84." Regarding claim 97, the Examiner asserts that this claim is ambiguous because it is unclear what properties compatible with the active compound are referred to. As to claim 99, the Examiner asserts that this claim is ambiguous because of the phrase "significant amount." The Examiner asserts that claims 100 and 109 are ambiguous because it is unclear what specific physiological disorders are being claimed. Regarding claim 108, the Examiner asserts that this claim is ambiguous because it is unclear how one monitors aggressiveness of a tumor based on the steps recited in claim 96.

In view of the following, this rejection is respectfully traversed.

Claim 84 has been amended to included the definition of R described in the specification at page 2, paragraph 26. Further, the term "comprises" has been replaced with the term "is selected from the group consisting of" to provide proper

Markush terminology. The recitation of "a label capable of undergoing an enzymatic reaction that produces a detectable color" has been deleted.

With regard to claim 96, claim 96 has been amended to delete the recitation of "said metal being comprised within the Q moiety of the compound of claim 84."

Claim 97 has been amended to delete the recitation of an active compound.

Claim 99 has been canceled without prejudice or disclaimer.

Claim 108 has been amended to delete the recitation of "aggressiveness of a tumor."

Regarding claims 100 and 109, Applicants assert that these claims are clear and definite within the meaning of 35 USC § 112, second paragraph. Claim 109 is dependent on claim 100. Claim 100 is directed to a method for the detection of physiological disorders characterized by the presence of cells having perturbed membranes (PM cells). Claim 100 is not ambiguous because it clearly describes that the physiological disorders are those characterized by the presence of cells having perturbed membranes. PM cells and physiological disorders characterized by the presence of these cells, are described in the specification at, for example, pages 13-14 and 16-17, as well as in the claims as originally filed. In addition, please see the above discussion directed to enablement.

Claim 110 has been newly added. Support for this claim is found throughout the specification, specifically at page 5, paragraph 66, which describes a method for detection of PM cells where cells are detected by comparing the amount of agent bound to cells in a sample with an amount of the agent bound to a control cell, i.e. cells that maintain their normal membrane organization, wherein if more of the agent is bound to the cells in the sample than the amount of agent bound to the control cell, the cells are detected as being PM cells: "*One desired property of the*

compounds of the present invention, is the selective binding of said compounds to membranes of cells, undergoing perturbation of their normal plasma membrane organization (PNOM), with potential subsequent entry into and accumulation within said cells; while essentially binding/accumulating substantially less within cells maintaining their normal membrane organization. This property may be useful for the detection of cells or cell-derived particles, which contain PNOM membranes (PM)."

Further support is found in the description of Figs. 2 and 3 (page 8, paragraphs 140 and 144, respectively) and Examples 4-7, which show selective binding of a compound of the invention to a PM cell more than amount of the compound bound to a control cell.

In view of the foregoing, it is submitted that claims 84, 96, 97, 99, 100, 108, and 109 are clear and definite within the meaning of 35 USC § 112, second paragraph. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

III. At page 8, item 10, of the Official Action, the Examiner requests certain claim amendments.

The Examiner requests that claim 84 be amended to replace the term "including" with the term "comprises"; replace "among" in claims 85 and 95 with "from the group consisting of" and replace "including with "and"; replace "including" with "and" in claims 86-88, 90, 91, 92, 93, and 94; in claim 98, after "is" insert "selected from the group consisting of"; in claim 99, delete the extra ".; and in claims 105 and 107 replace "among" with "from."

Applicants thank the Examiner for the above suggestions. Claims 84-88, 90-95, 105 and 107 have been amended as suggested.

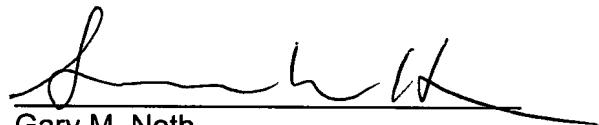
CONCLUSION

In view of the foregoing, Applicants submit that the application is in condition for allowance. Early notice to that effect is earnestly solicited. The Examiner is invited to contact the undersigned attorney if it is believed that such contact will expedite the prosecution of the application.

In the event this paper is not timely filed, Applicants hereby petition for an appropriate extension of time. Please charge any fee deficiency or credit any overpayment to Deposit Account No. 14-0112.

Respectfully submitted,

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